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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/230,955	05/04/99	MASON R	A-67653/DCA/

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EXAMINER	
BRUMBACK, B	
ART UNIT	**PAPER NUMBER**
1642	7

DATE MAILED: 09/27/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/230,955	Mason et al.
Examiner	**Group Art Unit**
Brenda Brumback	1642

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-9 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's preliminary amendment filed 02/04/1999 (Paper # 5) is acknowledged. Claims 4 and 9 were amended. Pending claims are 1-9.

Information Disclosure Statement

2. The Information Disclosure Statement filed 07/01/1999 has been entered as Paper # 6. A signed copy is attached hereto.

Claim Objections

3. Claims 1-9 are objected to because they lack proper introduction. The present Office practice is to insist that each claim be the object of a sentence starting with a phrase such as "I (or we) claim" or "What is claimed is" or "That which is claimed is". See MPEP 608.01 (m). Appropriate correction is required.

4. The date of deposit of deposited cell lines and the address of the depository are generally not included in a claim reciting the cell lines by accession number. It is suggested that the date and address be deleted from claims 3, 5, and 7. Furthermore, for clarity it is suggested that each of the accession numbers be preceded by the acronym "ECACC", *i.e.*, ECACC 95020718, ECACC 95020716, etc.

Specification

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

6. The use of the trademark TEXAS RED® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112/101

7. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 are indefinite in that they lack a contacting and a correlation step. While it is not necessary that a claim list every step of the claimed method in detail; a preamble, at least one active method step (the contacting step) and a correlation step are required.

Claim 1 is drawn to a method of determining abnormality in a tissue sample. Recitation of "abnormality" renders the claim indefinite because the disclosure fails to teach the meaning of the term other than as "some deviation from normality" (see page 1, lines 5-6). While the disclosure

teaches certain specific abnormal conditions as premalignant or neoplastic cellular changes, other types of abnormalities are not defined. Therefore, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Claims 1-4 and 6-8 recite "specific binding substances"; this phrase renders the claims indefinite because the disclosure fails to teach the metes and bounds of such substances. While monoclonal antibodies are disclosed as one category of specific binding substance, no other categories are described. Absent such a disclosure, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Claims 2-4 and 7 recite substances which "include"one or more polypeptides or which "include" an immunoglobulin binding domain. The term "include" connotes that the element may be a minor element of the composition, rather than an important component. It is suggested that the judicially preferred term "comprise" be substituted for "include".

Claims 3, 6, and 7 recite an "immunoglobulin antigen binding domain obtainable" from recited hybridomas. The art teaches that monoclonal antibodies are obtained from hybridomas. While it is recognized in the art that antibodies comprise an antigen binding domain, it is not clear how the antigen binding domain itself is obtainable from a hybridoma. Thus the claims are indefinite.

In claim 4, line 2, "complete" appears to be a typographical error for "compete". Correction is required.

Claims 4 and 8 recite substances which "compete" for binding to cervical tissue. While it is known that antibodies will compete with each other for binding sites, the nature of what other substances would be encompassed within claims 4 and 8 is unclear. The disclosure fails to provide guidance as to what other types of substances would compete with antibodies obtained from the recited hybridomas and thus the claims are indefinite.

Claims 4, 6, and 7 recite substances "obtainable" from a hybridoma. The term "obtainable" renders the claims indefinite because it cannot be determined if such substances are actually obtained from the hybridomas or from some other undefined source.

It appears that claim 5 is missing the phrase "under the accession numbers" between lines 4 and 5.

Claim 6 recites a hybridoma and/or an immunoglobulin antigen binding domain. The "and/or" renders the claim indefinite because it is unclear if the claim is intended to encompass a hybridoma, an immunoglobulin antigen binding domain, or both simultaneously. Correction is required.

Claims 6 and 9 provide for the use of a hybridoma or a specific binding substance obtainable from the hybridoma, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 6 and 9 are also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 9 is indefinite for recitation of "assessment of the nature or condition of cells". The disclosure fails to teach the parameters of such "nature or condition" and thus the claims are indefinite.

8. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining changes in cells of the cervix indicative of a premalignant or neoplastic condition or disease comprising determining binding of specific monoclonal antibodies to the cells in a sample and comparing the binding the pattern of binding in normal cervical cells, does not reasonably provide enablement for a method of determining any abnormality in a tissue sample containing cells of the cervix. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. Among the factors to be considered in determining whether a disclosure meets the enablement requirement are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The claimed invention is drawn to a method of determining abnormality in a tissue sample containing cells of the cervix comprising determining binding of specific binding substances to the sample and comparing the binding of these substances in the sample to the pattern of binding in a normal cervical cell sample. The art teaches that abnormalities in cervical cells may be due to premalignant or malignant changes or that they may be due to unrelated conditions, such as infection, for example. The art teaches that premalignant and malignant changes may be elucidated by staining for tumor markers or other cellular markers using monoclonal antibodies (see GB 2 215 046, of record as reference C in paper # 6, the abstract). The art does not teach detection of abnormalities due to an infection, such as bacterial infection, by contacting the cells with specific binding substances. Rather, the art teaches diangosis by a wet mount or Papanicoulaou smear (see Eltabbakh et al., Obstetrics and Gynecology 85(4):499-503, 1995, the abstract). Thus, the art teaches that not all abnormalities in cells of the cervix are elucidated using specific binding substances. The instant disclosure teaches staining cervical samples with specific

monoclonal antibodies for detection of cellular markers which differ between normal and premalignant or neoplastic cells. The working examples are all directed to the use of monoclonal to detect these markers. There is no guidance as to how to use the monoclonal antibodies for detecting other types of abnormalities in cervical cells, such as abnormalities due to bacterial infection, for example. Because the claims are broadly drawn to determining abnormality of any type, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims. Additionally, because the claims are broadly drawn to determination of abnormalities comprising contacting cells with specific binding substances, and the specification is restricted to disclosure of specific monoclonal antibodies, it would require undue experimentation by one of skill in the art to be able to determine what binding substances other than monoclonal antibodies could be used to practice the claimed methods.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by any of Kerr et al. (UK 2 215 046), Porta et al. (Pat. Clin. Ost. Gin., 14:348-355, 1986; of record as reference 5 in paper # 6), Kamiya et al. (Acta Cytologica, 37(2):131-134, 1993), or Smedts et al. (American Journal of Pathology, 142(2):403-412, 1993).

The claimed invention is drawn to a method of determining abnormality in a sample of cervical cells comprising determining the binding of specific binding substances having immunoglobulin antigen binding domains with the sample of cervical cells and comparing the binding to that with normal cervical cells.

Kerr et al. teach determination of cervical intraepithelial neoplasia comprising staining cervical tissue cells with a monoclonal antibody to the CD15 antigen (any monoclonal antibody comprises an immunoglobulin antigen binding domain) and comparing the amount of staining with that of normal tissue (see the abstract).

Porta et al. teach determination of carcinoma of the cervix comprising staining cervical cells with monoclonal antibodies to identify abnormal patterns of antigen expression in neoplastic cervical epithelial cells (see the abstract).

Kamiya et al. teach detection of cervical small cell undifferentiated carcinoma comprising staining samples of cervical cells with monoclonal antibodies against cluster 1 small cell lung cancer (SCLC) antigen and comparing the staining pattern to non-small cell cervical cancers (see the abstract).

Smedts et al. teach determination of cervical neoplasia and carcinoma comprising determining the binding of monoclonal antibodies directed against specific keratins with samples of cervical cells and comparing the pattern of expression of the keratins in the sample with the patterns of expression in normal and malignant cells (see the abstract and page 403, first paragraph).

Claim Rejections - 35 USC § 102/103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over any of Kerr et al., Porta et al., Kamiya et al., or Smedts et al.

The claimed invention is drawn to a method of determining abnormality in a sample of cervical cells comprising determining the binding of substances to cervical cells in a sample which compete with the binding of one or more of the specifically recited monoclonal antibodies and comparing the binding to that with normal cervical cells.

As outlined *supra*, any of Kerr et al., Porta et al., Kamiya et al., or Smedts et al. teach determining abnormality in a sample of cervical cells comprising contacting the sample with one or more monoclonal antibodies and comparing the binding of the monoclonal antibodies to the cells in the sample with the pattern of binding to normal cells. Because any of Kerr et al., Porta et al., Kamiya et al., or Smedts et al. teach monoclonal antibodies which bind to the cells in the sample, in sufficient quantities these monoclonal antibodies would inherently interfere or compete with the binding of other monoclonal antibodies due to stearic hindrance.

Conclusion

11. No claims are allowed.

12. Claims 3, 5-7 and 9 are free of the art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a

Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.
BB
September 22, 2000

Brenda Brumback
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Patent Examiner